American Journal of Hematology 58:255–262 (1998)

Predictive Parameters for Mobilized Peripheral Blood CD34+ Progenitor Cell Collection in Patients With Hematological Malignancies

Giovanni D'Arena,[1]* Pellegrino Musto,[1] Lazzaro Di Mauro,[2] Nicola Cascavilla,[1] Nicola Dello Iacono,[2] Potito Rosario Scalzulli,[1] Rosella Matera,[1] and Mario Carotenuto[1]

[1]Division of Hematology, IRCCS ''Casa Sollievo della Sofferenza'' Hospital, San Giovanni Rotondo, Italy
[2]Transfusional Service, IRCCS ''Casa Sollievo della Sofferenza'' Hospital, San Giovanni Rotondo, Italy

In order to investigate what is the best single parameter to predict the leukapheretic yield of circulating CD34+ progenitor cells, we retrospectively analyzed data from 68 patients with hematological malignancies who underwent mobilizing therapy. Three main parameters were monitored: total white blood cell (WBC), CD34+ cells, and monocyte counts in peripheral blood (PB) at the same day and at the preceding day of the apheretic procedure. Linear regression analysis revealed a strong correlation between CD34+ cell value in PB just before harvest and the number of CD34+ cells collected ($P < 0.0001$), but not at the preceding day. Monocyte PB concentration and absolute WBC count did not correlate with CD34+ cells harvested, at the preceding day of leukapheresis as well as at the same day of the procedure. The number of CD34+ cells in mobilized PB at the same day of harvest evidenced a very good capacity of predicting the value of harvested CD34+ cell number after collection, while WBC and monocyte count displayed quite a wide dispersion of results. In particular, an amount greater than 50/μL of circulating CD34+ cells ensured the best collections. Finally, CD34+ and CFU-GM content evaluated for each apheresis showed a strong reciprocal correlation (r 0.78; $P < 0.0001$). We conclude that the absolute number of CD34+ cells at the day of leukapheresis is the only parameter for identifying the exact timing for apheresis and predicting the amount of peripheral blood progenitor cells (PBPCs) that will be collected. In this setting, WBC and monocyte counts, at the day of collection or at the preceding day, are not useful tools. Am. J. Hematol. 58:255–262, 1998. © 1998 Wiley-Liss, Inc.

Key words: CD34+ peripheral blood progenitor cells; mobilizing therapy; leukapheresis; monocyte count; white blood cell count; flow cytometry

INTRODUCTION

Hematopoietic progenitor cells, identified by the expression of CD34 surface antigen, are present in bone marrow (BM) and can be detected in steady state peripheral blood (PB), though at a very low level. During the recovery phase from non-ablative chemotherapy administration, there is a well-documented increase in the number of CD34+ peripheral blood progenitor cells (PBPCs) [1] that can be further enhanced by adding growth factors, such as granulocyte colony stimulating factor (G-CSF) or granulocyte-macrophage colony stimulating factor (GM-CSF) [2–4]. These cells can be estimated by flow cytometry [5,6] and their large-scale collection requires leukaphereses, often performed on consecutive days if their blood levels remain high. Cryopreserved for transplantation, PBPCs are able to engraft and to restore the hemopoiesis after myeloablative therapy [7–9].

However, the rise of PBPCs is of short duration after the phase of mobilization. Thus, it is crucial to begin leukaphereses during this period, when an important overshoot of PBPCs appears. In addition, optimal timing and number of leukaphereses that need to be performed are essential in all patients to obtain a sufficient amount of PBPCs CD34+ for a safe autografting. In this setting,

*Correspondence to: Giovanni D'Arena, M.D., Hematology Division, IRCCS ''Casa Sollievo della Sofferenza'' Hospital, 71013 San Giovanni Rotondo, Italy.

Received for publication 22 January 1997; Accepted 18 March 1998

TABLE I. Patients Undergoing Mobilizing Therapy According to Diagnosis

Multiple myeloma (MM)	21
Acute myeloid leukemia (AML)	18
Non-Hodgkin lymphoma (NHL)	19
Hodgkin disease (HD)	9
Waldenström's macroglobulinemia	1
Total patients	68

TABLE II. Mobilizing Regimens Used*

Cyclophosphamide 7 g/sqm	48
Modified EDAP	12
DEXA-BEAM	8
Ara-C + Mitoxantrone	9
FLAG	5
Idarubicin + Ara-C + Etoposide	8
Etoposide 2 g/sqm	5
BCNU + Cisplatin + Etoposide	1
Only G-CSF	1
Total cycles performed	97

*All regimens included G-CSF or GM-CSF at the daily dose of 5 μg/kg.

the absolute white blood cell (WBC) and monocyte count, as well as their rate of increase, have been used to guide apheretic procedures [2,10–13].

The degree of mobilization and the yield of PBPCs collected are correctly quantified by the level of clonogenic cells as detected by colony-forming units granulocyte-macrophage (CFU-GM) or CD34+ cell estimation by flow cytometry. However, the information on CFU-GM levels is available only after 2 weeks, while the flow cytometric estimation is performed in about 1 h, thus allowing the avoidance of useless leukaphereses if sufficient PBPCs are collected and providing information comparable to that obtained with CFU-GM assay, as we and others have previously shown [6,14–17].

In the present study, we have retrospectively analyzed data from 68 patients with hematological malignancies who underwent mobilizing chemotherapy, to compare the capacity of predicting PBPCs' leukapheretic yield of circulating CD34+ cells, WBC, and monocyte daily estimation.

PATIENTS AND METHODS

Patients and Aphereses

At our Institution, from April 1993 to August 1996 a total of 68 patients, with a median age of 40.7 years (range 4–65), underwent mobilizing treatments for collecting PBPCs by leukaphereses to utilize after high-dose chemotherapy. The underlying diagnoses are listed in Table I and the mobilizing chemotherapy regimens used are listed in Table II. Harvests were performed, after informed written consent, with a CS3000 plus (Baxter, Columbia, MD) or an MCS (Haemonetics, Braintree, MA) cell collector, using a target processing of about 9 liters at a flow rate of 40–80 ml/min.

The aphereses were usually started when a WBC count greater than 1,000/μL was reached and when the absolute number of CD34+ cells in the blood exceeded 20/μL. In one patient, suffering from acute myeloid leukemia in first remission, only G-CSF was used and the aphereses were started on day 6. The possibility to perform a collection even though circulating CD34+ cell concentration was below 20/μL was always considered in relation to the particular clinical history, state of disease, and therapeutic strategy adopted.

Some patients received multiple different mobilizing cycles (i.e., myeloma patients were enrolled in a protocol in which three cycles, high-dose cyclophosphamide, EDAP, DEXA-BEAM, were programmed in sequence).

Cell Count and Flow Cytometry

The patients were closely followed with daily WBC and leukocyte subsets monitoring from the start of mobilization therapy until the end of the apheretic procedure. The leukocyte absolute and differential count in the samples was determined by a Coulter STKS (Coulter Diagnostics, Hialeah, FL). For CD34+ PBPCs estimation, we used a flow cytometric method, according to the Milan Protocol, as described by Siena and co-workers [5, 18,19].

Briefly, 100 μL of whole mobilized PB or leukapheresis sample was incubated at 4°C in the dark for 25 min with 10 μL fluorescein (FITC)- or phycoerythrin (PE)-conjugated anti-CD34 monoclonal antibody HPCA-2 (Becton Dickinson, San Jose, CA). After red blood cells lysing (Lysing Solution, Ortho Diagnostic, Raritan, NJ) and twice washing by centrifugation in Phosphate-Buffered Saline (PBS) containing 0.1% sodium azide and 0.5% bovine serum albumin, the samples were stored and analyzed by flow cytometry. Data were acquired on a FACSort flow cytometer (Becton Dickinson) equipped with a 15 mW Argon Laser emitting at 488 nm and Lysis II software. All channels were set for acquisition in the logarithmic mode. CD34+ cell frequency estimation was performed on a total of 10,000 cells, using a scattergram with the horizontal axis as side (90°) light scatter and the vertical axis as fluorescence (red or green). Using this technique, true CD34+ cells form a discrete cluster that exhibits low-density CD34 expression and low-side scatter characteristics (Fig. 1). Mouse IgG_1 and IgG_2 (γ_1 and γ_2, Becton Dickinson) were used as isotypic controls to determine background fluorescence.

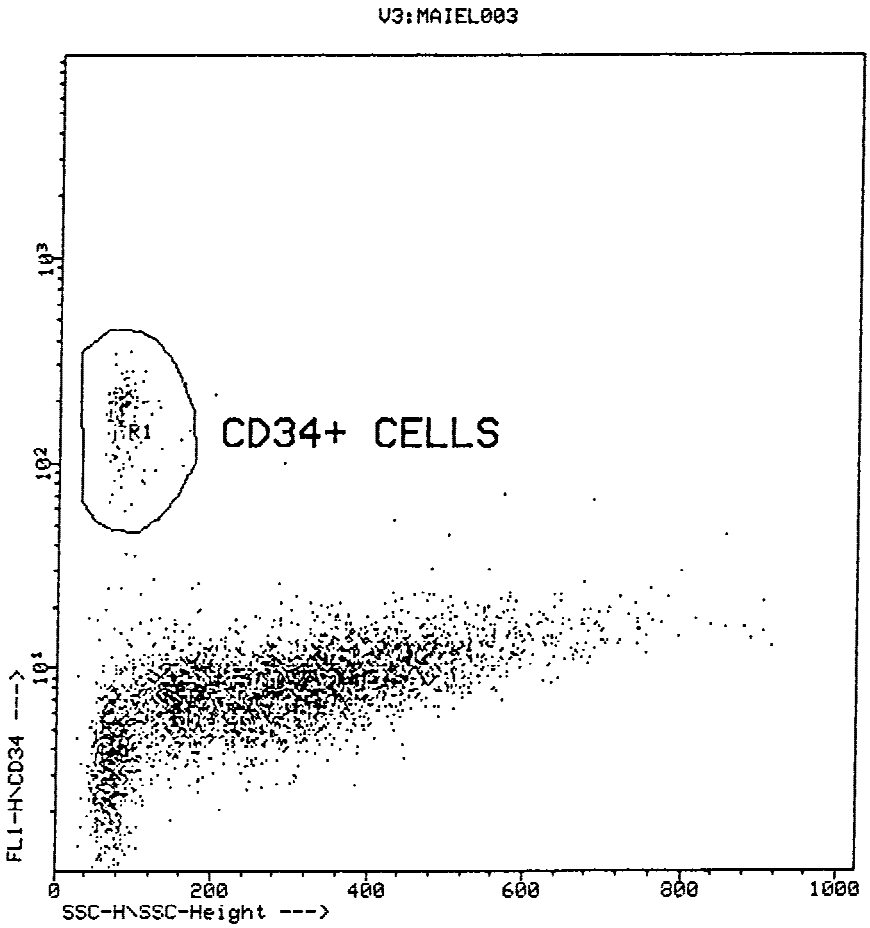

Fig. 1. Dot plot generated by combining right angle side scatter on the horizontal axis and green fluorescence (FITC-conjugated CD34) on the vertical axis. The CD34+ cells form a well-defined discrete cluster (gated) separated from the negative autofluorescent cells.

TABLE III. Leukapheretic Collection Data*

Performed procedures	164
Procedures per patient	2 (range 1–4)
MNC ($\times 10^8$/kg)	1.27 (range 0.2–16.1)
CFU-GM ($\times 10^4$/kg)	6.41 (range 0.3–31)
CD34+ cells ($\times 10^6$/kg)	3.74 (range 0.05–20)

*Data are expressed as mean number of each value.

CFU-GM Assay

Mononuclear cells (MNCs) from leukapheresis samples were isolated by centrifugation over a density gradient (Lymphoprep); thereafter they were washed two times in PBS. The MNCs were then diluted in culture medium (Iscove's MDM) and 5×10^5 cells were plated on Iscove's methylcellulose cultures containing 30% fetal calf serum, 10% bovine serum albumin, 2 U/μL erythropoietin, 50 ng/μL GM-CSF, and 10^{-4} μL β-mercaptoethanol. After incubation at 37°C in a humidified atmosphere of 5% CO_2 in air, CFU-GM were counted in duplicate with an inverted microscope 14 days after initiation of cultures.

Statistical Analysis

Simple linear regression analysis and Pearson's correlation test were used to establish relationships between the evaluated parameters.

RESULTS

A total of 164 leukaphereses, whose main characteristics are reported in Table III, was retrospectively analyzed. Twelve patients (7 AML, 3 MM, 2 NHL) failed mobilization. In general, they were heavily pre-treated and often showed myelodysplastic features in the marrow, factors that have been previously described as negatively influencing collections [20–22]. Four MM patients failed to complete the programmed third cycle of mobilization (DEXA-BEAM), after two effective collections with cyclophosphamide and EDAP. A fifth patient with MM failed at the second cycle (EDAP).

The mean number of leukaphereses performed on consecutive days for each cycle was 2 (range 1–4). Leukaphereses were started after a mean of 13.8 days (range

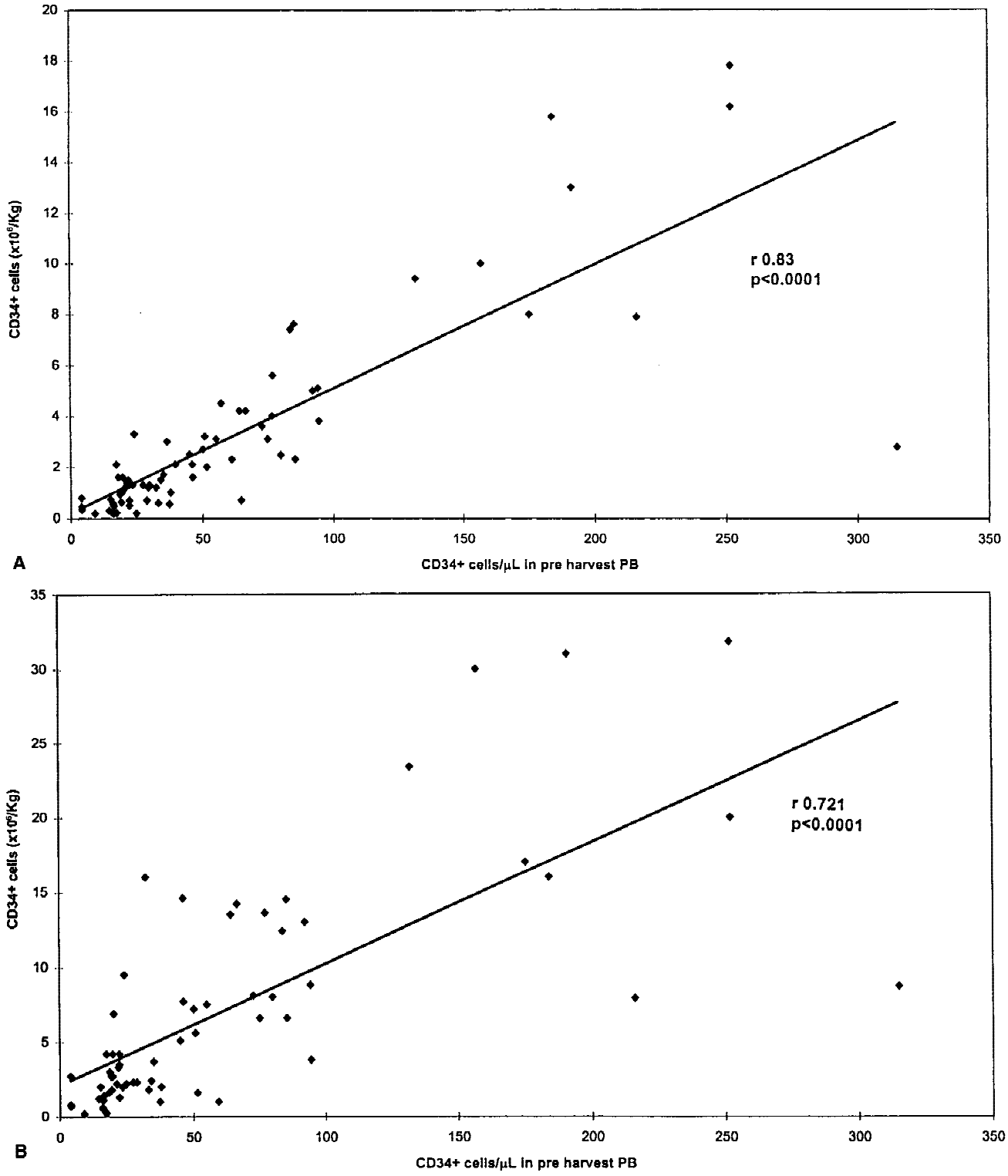

Fig. 2. Linear regression analysis. Harvest-day PB CD34+ cell concentration vs. CD34+ cells collected after the first apheresis (A) and after the total number of aphereses performed in single patients (B).

TABLE IV. CD34+, WBC, and Monocyte Absolute Number (/μL) at the Preceding and at the Same Day of Leukapheresis: Correlation With CD34+ Cell Collected (×10^6/kg)*

Parameters	Correlation (*R*)	Statistics (*P*)
CD34+ cells pre-harvest	0.839	<0.0001
CD34+ cells at the preceding day	0.17	ns
WBC pre-harvest	−0.001	ns
WBC at the preceding day	−0.125	ns
Monocytes pre-harvest	0.083	ns
Monocytes at the preceding day	−0.064	ns

*ns, not significant.

6–25), with a mean PB WBC count of 6,723/μL (range 1,000–37,300) at the same day of procedure. Pre-harvesting PB samples showed mean monocyte and CD34+ cell counts of 725/μL (range 70–5,329) and 65/μL (range 4–336), respectively. In the AML patient mobilized with G-CSF alone, the first harvest was performed on day 6 (WBC: 37,300/μL; monocytes: 1,044/μL; CD34+ cells: 37/μL). Regarding the day preceding the harvest, we found 2,692/μL (range 200–40,600) as the mean WBC number, 17/μL (range 0.03–164) as the mean CD34+ cell number, and 384/μL (range 22–3,078) as the mean monocyte number.

Linear regression analysis performed using blood parameters documented prior to the first apheresis (''decision point'') revealed a strong correlation between CD34+ cells in pre-harvesting PB at the same day of the procedure and the amount of CD34+ PBPC collected (Fig. 2 and Table IV), but not at the preceding day (Table IV). PB monocyte concentration and absolute WBC count did not show a direct correlation with CD34+ cells harvested, both at the day of leukapheresis and at the preceding day (Table IV). Figure 3A–F, which includes all leukaphereses performed, clearly shows that a high number of CD34+/μL in mobilized PB at the same day of harvest evidenced a significant correlation with the distribution of harvested CD34+ cell number after collection, whereas WBC and monocyte count displayed a wider dispersion of values. In particular, it appeared that an amount greater than 50/μL of circulating CD34+ cells ensured a minimum of 2×10^6 kg cells collected in almost all cases.

Finally, both CD34+ cell and CFU-GM assay were available on 137 leukapheretic harvests and a strong correlation (r: 0.78; $P < 0.0001$) was found between these two parameters (Fig. 4).

DISCUSSION

PBPCs transplantation is now increasingly used as rescue after high-dose cytotoxic therapy, instead of BM, because of a rapid hematological recovery that leads to a decreased toxicity, with reduced requirement of antibiotics and blood-products and shorter hospitalization. The possibility of a lower neoplastic contamination with respect to BM has also been claimed, though not formally proved.

In this setting, it is crucial to optimize the harvesting procedure, searching the optimum time to start PBPC collection in order to obtain an adequate product. Clonogenic assays have so far represented the standard reference method, but they require 2 weeks to be completed. This problem can be overcome by flow cytometric assessment of CD34+ cells in mobilized PB, since, as we also observed, a close linear relationship exists between the number of CD34+ cells and day 14 CFU-GM present in the leukapheretic samples [6].

In the present study we compared the predictive capacity of PB CD34+ cell evaluation with that of more simple parameters, such as WBC and monocyte count. Our data show that the only predictive parameter for PBPCs harvest remains the absolute CD34+ cell number in PB just before leukapheresis, while CD34+ value in the preceding day is not significant. Both WBC and monocyte count at the same day when leukapheresis is performed or at the preceding day also were not relevant in predicting leukapheretic yield.

Some controversies still exist about the threshold dose of CD34+ PBPC number that should be infused for a safe engraftment. Some authors indicate the number of 2×10^6/kg body weight. However, more recently it has been claimed that CD34+ cell doses lower than 5×10^6/kg, although frequently successful, expose a fraction of patients to the risk of delayed or defective platelet reconstitution. In this regard, doses higher than 8×10^6/kg are probably required for the best results in terms of rapid, complete, and sustained hematopoietic reconstitution of myeloablated hosts [20–23].

At our institution, leukaphereses are usually started when CD34+ and WBC in PB are more than 20/μL and 1,000/μL, respectively [24]. Although the analysis on data obtained from 164 aphereses showed that the best leukapheretic yields were obtained when CD34+ cells in PB were more than 50/μL, we should keep in mind that only the accurate evaluation of single patient's clinical history, together with laboratory data, must guide our clinical decisions. In fact, in patients with a history of heavy previous pretreatments, radiation therapy, myelodysplastic features, or exhausted bone marrow, in which we do not expect a rich collection, it is not wrong to perform a leukapheresis even though CD34+ cells in PB are very low. Though the quality of a leukapheresis does not depend only upon its CD34+ progenitor cell content [25–32], our data confirm [33] that also in these circumstances daily estimation of the circulating CD34+ cell

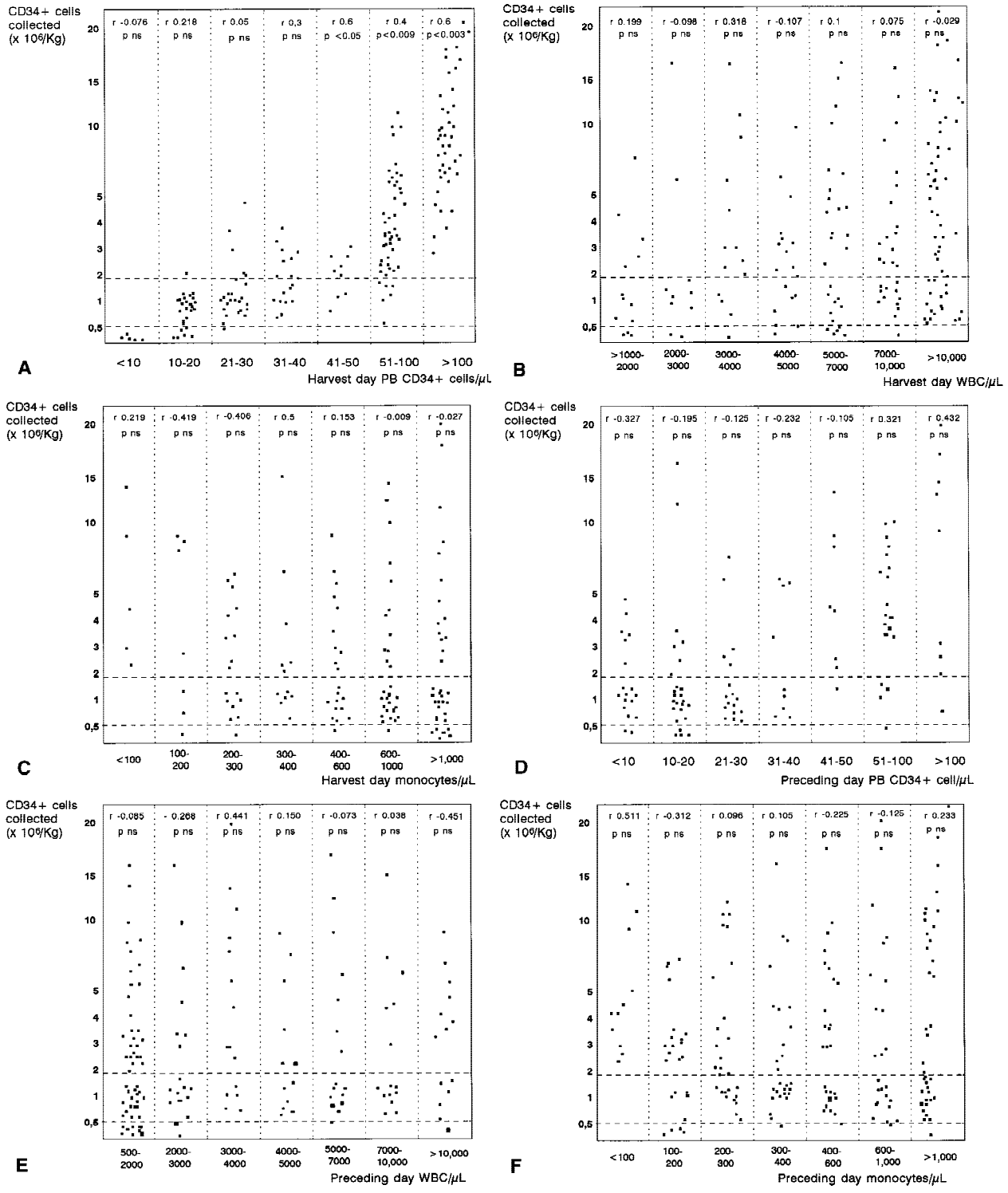

Fig. 3. Relationship between CD34+ cells harvest content and CD34+ cell, WBC and monocyte number at the same day (A, B, and C) and at the preceding day (D, E, and F) of leukapheresis.

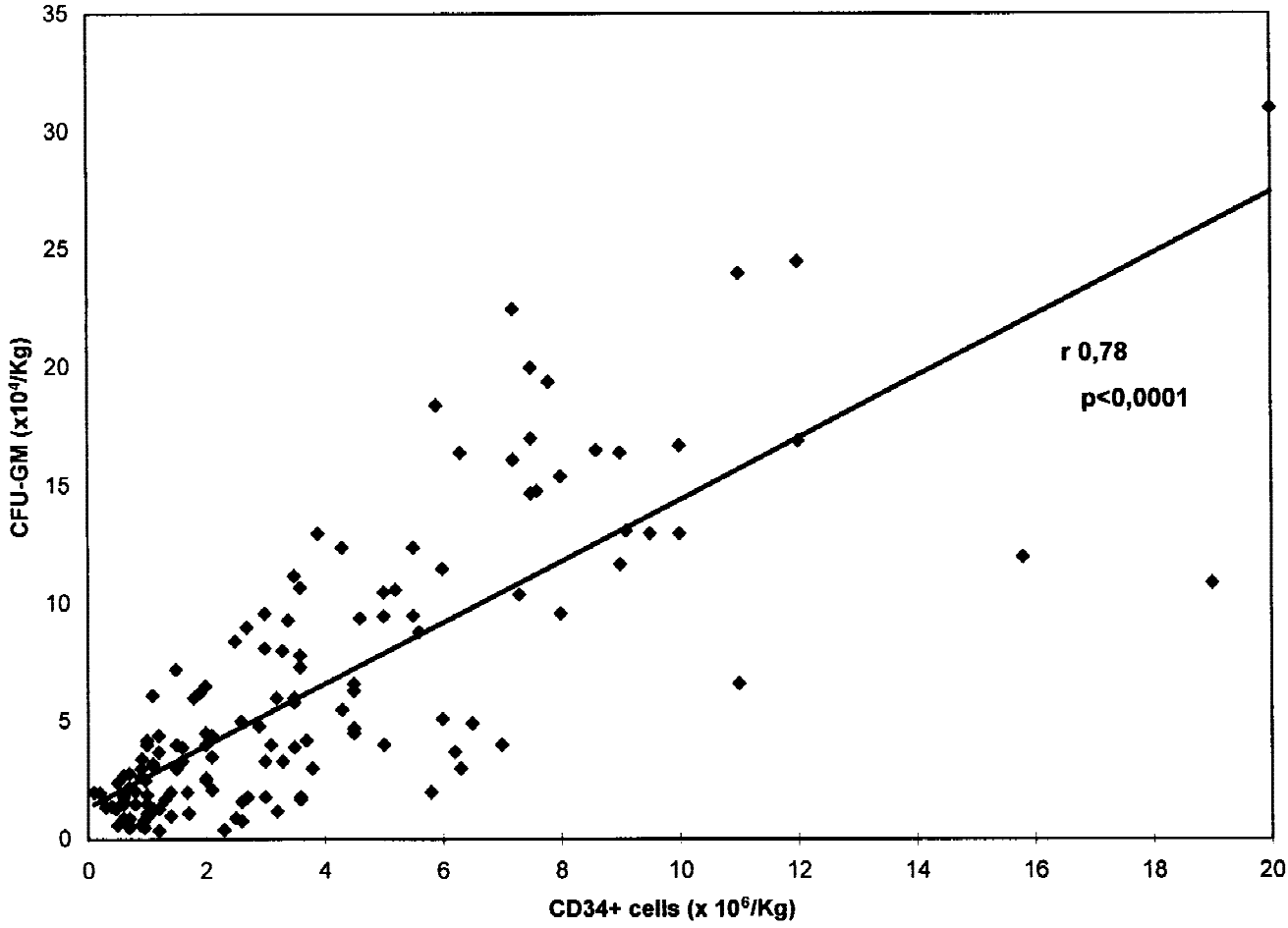

Fig. 4. Correlation between CD34+ cells and CFU-GM performed on leukapheretic products.

number by flow cytometry represents the best tool to guide a leukapheretic program.

REFERENCES

1. Richman CM, Weiner RS, Yankee RA: Increase in circulating stem cells following chemotherapy in man. Blood 47:1031, 1976.
2. Siena S, Bregni M, Brando B, Ravagnani F, Bonadonna G, Gianni M: Circulating of CD34+ hematopoietic stem cells in the peripheral blood of high-dose cyclophosphamide-treated patients: Enhancement by intravenous recombinant human granulocyte-macrophage colony-stimulating factor. Blood 74:1905, 1989.
3. Gianni AM, Siena S, Bregni M, Tarella C, Stern AC, Pileri A, Bonadonna G: Granulocyte-macrophage colony-stimulating factor to harvest circulating hematopoietic stem cells for autotransplantation. Lancet 2:508, 1989.
4. Peters WP, Rosner G, Ross M, Vredenbirgh J, Meisenberg B, Gilbert C, Kurtzberg J: Comparative effects of granulocyte-macrophage colony-stimulating factor (GM-CSF) and granulocyte colony-stimulating factor (G-CSF) on priming peripheral blood progenitor cells for use with autologous bone marrow after high-dose chemotherapy. Blood 81:1709, 1993.
5. Siena S, Bregni M, Brando B, Belli N, Ravagnani F, Gandola L, Stern AC, Lansdorp PM, Bonadonna G, Gianni AM: Flow cytometry for clinical estimation of circulating hematopoietic progenitor for autologous transplantation in cancer patients. Blood 77:400, 1991.
6. D'Arena G, Scalzulli P, Musto P: Circulating hematopoietic progenitor cells in leukapheresis: Flow cytometric estimation. Haematologica 81: 95, 1996.
7. Berenson RJ, Bensinger WI, Hill RS, Andrews RG, Garcia-Lopez J, Kalamsz DF, Still BJ, Spitzer G, Buckner DC, Bernstein ID, Thomas ED: Engraftment after infusion of CD34+ marrow cells in patients with breast cancer or neuroblastoma. Blood 77:1717, 1991.
8. Kessinger A, Armitage JO, Landmark JD, Smith DM, Weisenburger DD: Autologous peripheral hematopoietic stem cell transplantation restores hematopoietic function following ablative therapy. Blood 71: 723, 1988.
9. Williams SF, Bitran JD, Richards JM, DeCristopher PJ, Barker E, Conant J, Golomb HM, Orlina AR: Peripheral blood-derived stem cell collections for use in autologous transplantation after high-dose chemotherapy: An alternative approach. Bone Marrow Transplant 5:129, 1990.
10. To LB, Roberts MM, Haylock DN, Dyson PG, Brandford AL, Thorp D, Ho JQK, Dart GW, Norvath N, Davy MLJ, Olweny CLM, Abdi E, Juttner CA: Comparison of haematological recovery times and supportive care requirements of autologous recovery phase peripheral blood stem cell transplants, autologous bone marrow and allogeneic bone marrow transplants. Bone Marrow Transplant 9:277, 1992.
11. Kotasek D, Shepherd KM, Sage RE, Dale BM, Norman JE, Charles P, Grigg A, Pillow A, Bolton A: Factors affecting blood stem cell col-

lections after high-dose cyclophosphamide mobilization in lymphoma, myeloma and solid tumors. Bone Marrow Transplant 9:11, 1992.
12. Hansson M, Svensson A, Engervall P, Bjorkhol M, Gruber A, Soderstrom T: Increase of monocytes predicts mobilization of peripheral stem and progenitor cells after chemotherapy followed by G-CSF administration. Eur J Haematol 54:321, 1995.
13. Cagnoni PJ, Shpall EJ: Mobilization and selection of CD34-positive hematopoietic progenitors. Blood Rev 10:1, 1996.
14. Siena S, Bregni M, Gianni AM: Estimation of peripheral blood CD34+ cells for autologous transplantation in cancer patients. Exp Hematol 21:203, 1993.
15. Leibundgut K, von Rohr A, Brulhart K, Hirt A, Ischi E, Jeanneret C, Muff J, Ridolfi-Luthy A, Wagner HP, Tobler A: The number of circulating CD34+ blood cells predicts the colony-forming capacity of leukapheresis products in children. Bone Marrow Transplant 15:25, 1995.
16. Schots R, Van Riet I, Damiaens S, Flament J, Lacor P, Staelens Y, Steenssens L, van Camp B, De Waele M: The absolute number of circulating CD34+ cells predicts the number of hematopoietic stem cells that can be collected by apheresis. Bone Marrow Transplant 17:509, 1996.
17. Elliott B, Samson DM, Armitage S, Lyttelton MP, McGuidan D, Hargreaves R, Giles C, Abrahamson G, Abboudi Z, Brennan M, Kanfer EJ: When to harvest peripheral-blood stem cells after mobilization therapy: Prediction of CD34-positive cell yield preceding day CD34-positive concentration in peripheral blood. J Clin Oncol 14:970, 1996.
18. Siena S, Bregni M, Belli N, Ravagnani F, Notti P, Magni M, Di Nicola M, Bonadonna G, Gianni AM: Practical aspects of flow cytometry to guide large-scale collection of circulating hematopoietic progenitors for autologous transplantation in cancer patients. Intern J Cell Cloning 10(Suppl 1):26, 1992.
19. Siena S, Bregni M, Di Nicola M, Peccatori F, Magni M, Brando B, Ravagnani F, Gianni AM: Milan protocol for clinical CD34+ cell estimation in peripheral blood for autografting in patients with cancer. In Hematopoietic Stem Cells: The Mulhouse Manual. Dayton, OH: AlphaMed Press, 1994, p 23.
20. D'Arena G, Cascavilla N, Musto P, Greco M, Di Mauro L, Carella AM, Dello Iacono N, Carotenuto M: Flow cytometric characterization of CD34+ hematopoietic progenitor cells in mobilized peripheral blood and bone marrow of cancer patients. Haematologica 81:216, 1996.
21. Gordon MY, Blackett NM: Some factors determining the minimum number of cells required for successful clinical engraftment. Bone Marrow Transplant 15:659, 1995.
22. Gianni AM: Where do we stand with respect to the use of peripheral blood progenitor cells? Ann Oncol 5:781, 1994.
23. Siena S, Bregni M, Di Nicola M, Ravignani F, Peccatori F, Gandola C, Lombardi F, Tarella C, Bonadonna G, Gianni AM: Durability of hematopoiesis following autografting with peripheral blood hematopoietic progenitors. Ann Oncol 5:935, 1994.
24. D'Arena G, Musto P, Carotenuto M: When to perform peripheral blood progenitor cell collection in hematological patients? Haematologica 82:124, 1997.
25. Haas R, Mohle R, Fruhauf S, Goldschmidt H, Witt B, Flentje M, Wannenmacher M, Hunstein W: Patient characteristics associated with successful mobilizing and autografting of peripheral blood progenitor cells in malignant lymphoma. Blood 83:3787, 1994.
26. Bensinger W, Appelbaum F, Rowley S, Storb R, Sanders J, Lilleby K, Gooley T, Demirer T, Schiffman K, Weaver C, Clift R, Chauncey T, Klarnet J, Montgomery P, Petersdorf S, Weiden P, Witherspoon R, Buckner D: Factors that influence collection and engraftment of autologous peripheral-blood stem cells. J Clin Oncol 13:2547, 1995.
27. Demirer T, Buckner CD, Gooley T, Appelbaum F, Rowley S, Chauncey T, Lilleby K, Storb R, Bensinger WI: Factors influencing collection of peripheral blood stem cells in patients with multiple myeloma. Bone Marrow Transplant 17:937, 1996.
28. Carella AM, Podesta' M, Frassoni F, Raffo MR, Pollicardo N, Pungolino E, Vimercati R, Sassarego M, Parodi C, Rabitti C, Ferrero R, Benvenuto F, Figari O, Carlier P, Levcasic G, Valbonesi M, Vitale V, Giordano D, Pierluigi D, Nati S, Guerraçio A, Rosso C, Saglio G: Collection of normal blood repopulating cells during early hemopoietic recovery after intensive conventional chemotherapy in chronic myelogenous leukemia. Bone Marrow Transplant 12:267, 1993.
29. Gazitt Y, Reading CC, Hoffman R, Wickrema A, Vesole DH, Jagannath S, Condino J, Lee B, Barlogie B, Tricot G: Purified CD34 + Lin-Thy-1+ stem cells do not contain clonal myeloma cells. Blood 86:381, 1995.
30. Frassoni F, Carella AM: Collection, analysis and transplantation of Ph-negative blood precursor cells in chronic myeloid leukemia. Leukemia 10(Suppl 2):30, 1996.
31. Gazitt Y, Tian E, Barlogie B, Reading CL, Vesole DH, Jagannath S, Schnell J, Hoffman R, Tricot G: Differential mobilization of myeloma cells and normal hematopoietic stem cells in multiple myeloma after treatment with cyclophosphamide and granulocyte-macrophage colony-stimulating factor. Blood 87:805, 1996.
32. Caligaris Cappio F, Cavo M, De Vincentiis A, Lanuta L, Lemoli RM, Majolino I, Tarella C, Zanon P, Tura S: Peripheral blood stem cell transplantation for the treatment of multiple myeloma: Biological and clinical implications. Haematologica 81:356, 1996.
33. Armitage S, Hargreaves R, Samson D, Brennan M, Kanfer E, Navarrete C: CD34 counts to predict the adequate collection of peripheral blood progenitor cells. Bone Marrow Transplant 20:587, 1997.